SPECIFICALLY TARGETED ANTIBODY AGENT, COMPOSITION, KIT & RELATED USES

BACKGROUND OF THE INVENTION

Related Patents

This application is a divisional of US Patent Application Serial No. 08/482,596, filed June 7, 1995, which has been allowed; which in turn is a divisional of USSN 08/162,402 filed December 3, 1990, now US Patent No. 5,972,337; which is a continuation-in-part of USSN 07/607,538, now US Patent No. 5,455,031.

Technical Field

This invention relates to a polypeptide having the antibody binding specificity of the 46 kDalton HMFG differentiation antigen, a polynucleotide, and a polyribonucleotide encoding it, anti-polypeptide antibodies, methods of detecting the polypeptide and DNA and RNA encoding it, a method of imaging cells expressing the polypeptide, a method of detecting the presence of the polypeptide in a biological fluid by binding the antibody to the polypeptide, in vivo and ex vivo methods of delivering a therapeutic agent to a target cell expressing the polypeptide, a fusion protein of the polypeptide and at least one other polypeptide, labeled polynucleotides and polyribonucleotides encoding the polypeptide and a complementary DNA sequence, method of detecting RNA and DNA by hybridization with labeled probes, a method of vaccination with the polypeptide, and method of treating breast cancer with an anti-sense DNA.

WHAT IS SEEKED TO BE PATENTED AS NOVEL & UNOBVIOUS IN LETTERS PATENT OF THE UNITED STATES IS:

52. (Canceled)

53. (Canceled)

54. (Canceled)

55. (Canceled)

56. (Canceled)

57. (Canceled)

58. (Canceled)

59. (Canceled)

60. (Canceled)

61. (Canceled)

62. (Canceled)

63. (Canceled)

64. (Canceled)

65. (Canceled)

66. (Canceled)

81. (Amended) An in vivo method of imaging a cancer of epithelial origin or cells expressing a polypeptide having the antibody binding specificity of the about 46 Kd differentiation Human Milk Fat Globule (HMFG) antigen, comprising

administering to a subject suspected of being afflicted with the cancer or carrying the cells an amount of a detectably labeled or unlabeled specifically targeted antibody, comprising a monoclonal antibody selectively binding a 46 Kd MW HMFG differentiation antigen that has an antigen affinity constant about 10^{10}-10^{5} M^{-1}, and an agent comprising a detectable label, the antibody and the agent being operatively linked to one another, under conditions effective to deliver the antibody to target cells of epithelial origin carrying at least a portion of the 46Kd MW HMFG differentiation antigen in the subject's body to form antibody-cell antigen complexes;

administering to the subject a detectably labeled agent that binds the antibody at a site other than the 46 kDalton HMFG polypeptide binding site if the antibody is unlabeled; and

detecting the presence of a label in the subject's body.

82. (Amended) The method of claim 81, wherein the antibody is administered intravenously, intraperitoneally, intracavitarily, intra-tumor, intramuscularly, or into the lymphatic system.

83. (Amended) The method of claim 81, wherein the labeled agent comprises a fuorescent or radiolabeled agent.

84. (Amended) The method of claim 81, wherein

the antibody comprises an unlabeled antibody; and

the labeled agent comprises a labeled anti-antibody immunoglobulin, antibody binding fragment thereof, protein A, or Protein C.

85. (Amended) The method of claim 81, further comprising upon label detection the delivery of a therapeutic agent to target cancerous cells or cells of epithelial origin by

binding a therapeutic agent to the antibody of claim 81, at a site other than its antigen binding site;

administering to the subject a therapeutically effective amount of the antibody-bound therapeutic agent under conditions effective for the antibody to deliver the agent to the target cells; and

allowing the antibody to bind to the target cells, and the therapeutic agent to exert its effect on the cells.

86. (Canceled)

87. (Canceled)

88. (New) The method of claim 81, wherein the labeled agent comprises a radionucleide, a fluorescent label, an enzyme or biotin.

89. (New) The method of claim 81, wherein the labeled agent is detected as a conjugate.

90. (New) The method of claim 89, wherein the antibody is conjugated to avidin, streptavidin, or a magnetic bead.

91. (New) The method of claim 81, wherein the antibody comprises a monoclonal antibody.

92. (New) The method of claim 81, wherein the antibody is provided as a composition with a non -proteolytic carrier.

93. (New) The method of claim 92, wherein the carrier comprises a biologically acceptable carrier.

94. (New) The method of claim 93, wherein the carrier comprises a pharmaceutically acceptable carrier.

95. (New) The method of claim 85, wherein the therapeutic agent comprises a radionucleide, an immmunotoxin, or an enzyme.

96. (New) The method of claim 85, wherein the antibody-therapeutic agent is delivered as a conjugate.

97. (New) The method of claim 96, wherein the antibody-therapeutic agent is conjugated to avidin, streptavidin, or a magnetic bead.

98. (New) The method of claim 85, wherein the antibody-therapeutic agent comprises a monoclonal antibody.

99. (New) The method of claim 85, wherein antibody-therapeutic agent is provided as a composition with a non proteolytic carrier.

100. (New) The method of claim 99, wherein the antibody-therapeutic agent carrier comprises a biologically acceptable carrier.

101. (New) The method of claim 100, wherein the antibody-therapeutic agent carrier comprises a pharmaceutically acceptable carrier.

Table 1: DNA Sequence and Derived Amino Acid Sequence of BA46-1 cDNA.

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     *     10      *     20      *     30      *     40      *     50
GAT TTC ATC CAT GAT GTT AAT AAA AAA CAC AAG GAG TTT GTG GGT AAC TGG AAC
Asp Phe Ile His Asp Val Asn Lys Lys His Lys Glu Phe Val Gly Asn Trp Asn

*     60      *     70      *     80      *     90      *     100     *
AAA AAC GCG GTG CAT GTC AAC CTG TTT GAG ACC CCT GTG GAG GCT CAG TAC GTG
Lys Asn Ala Val His Val Asn Leu Phe Glu Thr Pro Val Glu Ala Gln Tyr Val

110     *   120     *   130     *   140     *   150     *   160
AGA TTG TAC CCC ACG AGC TGC CAC ACG GCC TGC ACT CTG CGC TTT GAG CTA CTG
Arg Leu Tyr Pro Thr Ser Cys His Yhr Ala Cys Thr Leu Arg Phe Glu Leu Leu

    *   170     *   180     *   190     *   200     *   210     *
GGC TGT GAG CTG AAC GGA TGC GCC AAT CCC CTG GGC CTG AAG AAT AAC AGC ATC
Gly Cys Glu Leu Asn Gly Cys Ala Asn Pro Leu Gly Leu Lys Asn Asn Ser Ile

   220     *   230     *   240     *   250     *   260     *   270
CCT GAC AAG CAG ATC ACG GCC TCC AGC AGC TAC AAG ACC TGG GGC TTG CAT CTC
Pro Asp Lys Gln Ile Thr Ala Ser Ser Ser Tyr Lys Thr Trp Gly Leu His Leu

     *     280     *     290     *     300     *     310     *     320
TTC AGC TGG AAC CCC TCC TAT GCA CGG CTG GAC AAG CAG GGC AAC TTC AAC GCC
Phe Ser Trp Asn Pro Ser Tyr Ala Arg Leu Asp Lys Gln Gly Asn Phe Asn Ala

*    330      *    340     *    350     *    360     *    370     *
TGG GTT GCG GGG AGC TAC GGT AAC GAT CAG TGG CTG CAG GTG GAC CTG GGC TCC
Trp Val Ala Gly Ser Tyr Gly Asn Asp Gln Trp Leu Gln Val Asp Leu Gly Ser

380     *   390     *   400     *   410     *   420     *   430
TCG AAG GAG GTG ACA GGC ATC ATC ACC CAG GGG GCC CGT AAC TTT GGC TCT GTC
Ser Lys Glu Val Thr Gly Ile Ile Thr Gln Gly Ala Arg Asn Phe Gly Ser Val

*   440     *   450     *   460 *       470     *   480     *
CAG TTT GTG GCA TCC TAC AAG GTT GCC TAC AGT AAT GAC AGT GCG AAC TGG ACT
Gln Phe Val Ala Ser Tyr Lys Val Ala Tyr Ser Asn Asp Ser Ala Asn Trp Thr

490     *   500   *     510     *   520     *   530     *   540
GAG TAC CAG GAC CCC AGG ACT GGC AGC AGT AAG ATC TTC CCT GGC AAC TGG GAC
Glu Tyr Gln Asp Pro Arg Thr Gly Ser Ser Lys Ile Phe Pro Gly Asn Trp Asp

          550     *   560     *   570     *   580     *   590
AAC CAC TCC CAC AAG AAG AAC TTG TTT GAG ACG CCC ATC CTG GCT CGC TAT GTG
Asn His Ser His Lys Lys Asn Leu Phe Glu Thr Pro Ile Leu Ala Arg Tyr Val

*   600     *   610     *     620     *   630     *   640     *
CGC ATC CTG CCT GTA GCC TGG CAC AAC CGC ATC GCC CTG CGC CTG GAG CTG CTG
Arg Ile Leu Pro Val Ala Trp His Asn Arg Ile Ala Leu Arg Leu Glu Leu Leu

650       *   660     *   670 *       680     *   690     *   700
GGC TGT TAG TGG CCA CCT GCC ACC CCC AGG TCT TCC TGC TTT CCA TGG GCC CGC    703
Gly Cys End   (SEQ. NO:2)

TGC CTC TTG GCT TCT CAG CCC CTT TAA ATC ACC ATA GGG CTG GGG ACT GGG GAA    757
GGG GAG GGT GTT CAG AGG CAG CAC CAC CAC ACA GTC ACC CCT CCC TCC CTC TTT    811
CCC ACC CTC CAC CTC TCA CGG GCC CTG CCC CAG CCC CTA AGC CCC GTC CCC TAA    865
CCC CCA GTC CTC ACT GTC CTG TTT TCT TAG GCA CTG AGG GAT CTG AGT AGG TCT    919
GGG ATG GAC AGG AAA GGG CAA AGT AGG GCG TGT GGT TTC CCT GCC CCT GTC CGG    973
ACC GCC GAT CCC AGG TGC GTG TGT CTC TGT CTC TCC TAG CCC CTC TCT CAC ACA   1027
TCA CAT TCC CAT GGT GGC CTC AAG AAA GGC CCG GAA GCC CCA GGC TGG AGA TAA   1081
CAG CCT CTT GCC CGT CGG CCC TGC GTC GGC CCT GGG GTA CCA TGT GCC ACA ACT   1135
GCT GTG GCC CCC TGT CCC CAA GAC ACT TCC CCT TGT CTC CCT GGT TGC CTC TCT   1189
TGC CCC TTG TCC TGA AGC CCA GCG ACA CAG AAG GGG GTG GGG CGG GTC TAT GGG   1243
GAG AAA GGG AGC GAG GTC AGA GGA GGG CAT GGG TTG GCA GGG TGG GCG TTT GGG   1297
GCC CTC ATG CTG GCT TTT CAC CCC AGA GGA CAC AGG CAG CTT CCA AAA TAT ATT   1351
TAT CTT CTT CAC GGG AAA AAA AAA AAA AAA ACC G                (SEQ. No. 1)  1382
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Potential n-linked glycosylation sites are underlined.

Table 2: Comparison of Derived BA46-1 Amino Acid Sequence with C-terminal Human Serum Factors V and VIII

46 Kda	F	I	H	D	V	N	K	K	H	K	E	F	V	G	N	W	N	K	N	A	V	H	V	N	L
FAV		F	K	G	N	S	T	R	N	V	M	Y	F	N	G	N	S	D	A	S	T	I	K	E	N	Q
FAVIII	Y	R	G	N	S	T	G	T	L	M	V	F	F	G	N	V	D	S	S	G	I	K	H	N	I
	F	E	T	P	V	E	A	Q	Y	V	R	L	Y	P	T	S	C	H	T	A	C	T	L	R	F	E	L	L	G
	F	D	P	P	I	V	A	R	Y	I	R	I	S	P	T	R	A	Y	N	R	P	T	L	R	L	E	L	G	K
	F	N	P	P	I	I	A	R	Y	I	R	L	H	P	T	H	Y	S	I	R	S	T	L	R	M	E	L	M	G
	C	E	L	N	G	C	A	N	P	L	G	L	K	N	N	S	I	P	D	K	Q	I	T	A	S	S	S	Y	K
	C	E	V	N	G	C	S	T	P	L	G	M	E	N	G	K	I	E	N	K	Q	I	T	A	S	S	F	K	K
	C	D	L	N	S	C	S	M	P	L	G	M	E	S	K	A	I	S	D	A	Q	I	T	A	S	S	Y	F	T
	T	W	G	L	H	L	F	S	W	N	P	S	Y	A	R	L	D	K	Q	G	N	F	N	A	W	V	A	G	S
	S	W	W	G	D	Y	-	-	W	E	P	F	R	A	R	L	N	A	Q	G	R	V	N	A	W	Q	A	K	A
	N	M	F	A	T	-	-	-	W	S	P	S	K	A	R	L	H	L	Q	G	R	S	N	A	W	R	P	Q	V
	Y	G	N	D	Q	W	L	Q	V	D	L	G	S	S	K	E	V	T	G	I	I	T	Q	G	A	R	N	F	G
	N	N	N	K	Q	W	L	E	I	D	L	L	K	I	K	K	I	T	A	I	I	T	Q	G	C	K	S	L	S
	N	N	P	K	E	W	L	Q	V	D	F	Q	K	T	M	K	V	T	G	V	T	T	Q	G	V	K	S	L	L
	S	V	Q	F	V	A	S	Y	K	V	A	Y	S	N	D	S	A	N	W	T	E	Y	Q	D	P	R	T	G	S
	S	E	M	Y	V	K	S	Y	T	I	H	Y	S	E	Q	G	V	E	W	K	P	Y	R	L	K	S	S	M	V
	T	E	M	Y	V	K	E	F	L	I	S	S	S	Q	D	G	H	Q	W	T	L	F	F	Q	N	-	-	G	K
	S	K	I	F	P	G	N	W	D	N	H	S	H	K	K	N	L	F	E	T	P	I	L	A	R	Y	V	R	I
	D	K	I	F	E	G	N	T	N	T	K	G	H	V	K	N	F	F	N	P	P	I	I	S	R	F	I	R	V
	V	K	V	F	Q	G	N	Q	D	S	F	T	P	V	V	N	S	L	D	P	P	L	L	T	R	Y	L	R	I
	L	P	V	A	W	H	N	R	I	A	L	R	L	E	L	L	G	C												**(SEQ. No. 3)**
	I	P	K	T	W	N	Q	S	I	A	L	R	L	E	L	F	G	C	D	-	-	-	I	Y					**(SEQ. No. 4)**
	H	P	Q	S	W	V	H	Q	I	A	L	R	M	E	V	L	G	C	E	A	Q	D	L	Y					**(SEQ. No. 5)**

An arrow indicates Junction of C1 and C2 repeats.